REMARKS/ARGUMENTS

I. Introductory Comments

This response follows the Decision on Appeal of June 22, 2005 wherein the Board affirmed by rejection of claims 16-21, 24 and 25 under 35 U.S.C. §102(b) over the McChesny *et al.* reference[1] based on a construction of the claims at pages 3-6 of the Decision. Claims 22 and 23 were rejected by the Board under 35 U.S.C. §103 based on the "combined" disclosures of Weithmann and Hammer *et al.* references.

Applicants have canceled claims 16-25 and request the addition of claims 26-34 to address the issues raised by the Board on Appeal.

II. Subject Matter of Applicants' Claims

Upon entry of the above-requested Amendment, new claims 26 through 34 will be pending in the Application. Sole independent claim 26 corresponds generally to prior claim 16 and is directed to Applicants' discovery that leflunomide products provide *in vivo* anti-viral effects in human patients. Unlike known anti-viral compounds which generally interfere with replication of viral DNA, leflunomide products, including those recited in new claims 27-28 (*c.f.*, prior claims 17-18), have been demonstrated by Applicants to interfere with the assembly, in the cell cytoplasm, of viral virion components such as viral DNA-containing nucleocapsids, tegument and external proteins. (*See* particularly Examples 5 and 8c.)

Anti-viral activity, including activity against a drug resistant virus, is demonstrated in the specification not only in the context of an *in vivo* animal model (Example 7) but in the successful treatment of a virally-infected human patient (page 46, line 13 through page 47, line 8) as recited in new claim 29 (*c.f.*, prior claim 25). In the animal and human studies, significant decreases in viral load were affected.

Dependent claims 30-32 generally correspond to prior claims 19-21 in their recitations of specific viral infectious agents and the text of claim 33 corresponds with prior claim 24 in its recitation of treatment of viruses resistant to inhibitors of viral DNA replication.

---

[1] While the Coghlan reference was mentioned in the Summary of the Board's decision at page 9 of the Decision, it was not applied or made part of the Board's statement of grounds for rejection at Decision pages 6-7.

Dependent claim 34 clarifies the effect of administering a pyrimidine, *i.e.*, as counteracting a potential side effect of claim 23 administration of leflunomide products by enhancing serum levels of uridine, cytidine or thymidine in circulation. Support for dependant claim 34 is found throughout the Application, particularly on pages 20 and 21.

III. Outstanding Rejections

Page 6 of the Decision that states:

> The examiner rejected claims 16-21, 24, and 25 as obvious in view of Coghlan and McChesney. We conclude that McChesney anticipates claim 16, as we interpret it, so we need not address Coghlan.

Therefore, claims 16-21, 24 and 25 stand rejected under 35 U.S.C. §102(b) in view of McChesney et al., "An Evaluation of Leflunomide in the Canine Renal Transplantation Model," *Transplantation, 57(No. 12)*:1717-1722 (1994) ("McChesney").

At pages 7-9 of the Decision, the Board rejected claims 22 and 23 under 35 U.S.C. §103 in view of Weithmann *et al.*, U.S. Patent No. 5,556,870 ("Weithmann") and Hammer, "Advances in Antiretroviral Therapy and Vial Load Monitoring," *AIDS, 10, (Suppl. 3)*:S1-S11 (1996) ("Hammer") based on a generalized motivation to combine anti-viral agents.

IV. Grounds for Reconsideration

A. The Section 102(b) Rejection Based on McChesney Is Not Applicable to Claims 26-34.

Applicants submit that no anticipation or obviousness rejection of the subject matter of new independent claim 26 can properly be drawn from McChesney.

McChesney evaluates the immunosuppressive effects of leflunomide alone and in combination with cyclosporine in dogs undergoing kidney allograft transplantation. The only mention in McChesney of viral infection is a statement in the abstract that, "Even at a high dose of 16mg/kg/day no viral or bacterial infections were noted." There is nothing reported in the article to support or explain this statement, which would be necessary in order to attribute the cause for such an observation to the administered drugs. Moreover, it is not surprising that McChesney noted this lack of viral infection. Institutional animal care guidelines (followed by

McChesney according to page 1721) require full vaccination of animals. (See Mocarski Declaration at paragraph 5.)

The cornerstone of the Board's rejection of prior claim 16 based on McChesney *et al.* was its "construction" that the claim did not require *in vivo* administration and, significantly, that the claim's preamble did not require that the recited contacting of cells "be done with the intent of inhibiting viral infection." (*See* Decision, page 5.) New claim 26 positively recites inhibition of viral infection by *in vivo* administration to human patients.

Because the McChesney reference does not address anti-viral treatment of humans and includes no experimental procedures for assessing anti-viral or antibacterial effects of leflunomide, it cannot properly be held to anticipate or render obvious the claimed subject matter of providing an anti-viral effect in a human patient by inhibiting viral virion assembly.

B. The Section 103 Rejection Based on Weithmann and Hammer Is Not applicable to New Claim 34.

Applicants submit that the subject matter of dependent claim 34 is not obvious in view of Weithmann and Hammer *et al.* references. Prior claim 22 (addressing use of anti-viral agents and leflunomide products) has been canceled. Claim 34 is dependent on claim 26, includes all the limitations thereof and is thus directed to co-administering a leflunomide product to a human patient (to obtain an anti-viral effect) along with a pyrimidine in an amount sufficient enhance serum levels of uridine, cytidine or thymidine. (*See* particularly pages 20 and 21 of the Application).

While Weithmann could be maintained to address "treating viral disorders," there is no teaching in Weithmann that any leflunomide product was known in the art to be useful as an "anti-viral agent" or to be "effective against virus" or to be capable of "inhibiting viral infection" as claimed by the Applicants. Rather, Weithmann describes *in vitro* tests of un-metabolized leflunomide (HWA 486) possessing activity in modulating the secretion of IL-1β by cells in patients having any number of diseases, including viral infections. There is no teaching in Weithmann that the un-metabolized leflunomide treats the viral diseases listed, only that IL-1β secretion might be modulated in patients with such diseases.

Weithmann does not teach any anti-viral effect of delivering leflunomide products or co-administering anti-viral agents with leflunomide products. Hammer's disclosure of co-administering multiple anti-viral agents does not supply the missing elements from Weithmann's

disclosure as it does not teach anti-viral effects for leflunomide products. Moreover, Hammer does not teach supplying pyrimidine compounds in amounts sufficient to enhance serum levels of uridine, cytidine or thymidine. Rather, Hammer only teaches pyrimidine compounds having the effect of inhibiting viral DNA replication – an effect opposite to that claimed.

V. Conclusion

The foregoing is believed to establish that claims 26-34 are in condition for allowance and an early notice thereof is solicited.

It is understood that no fees are necessary in connection with the present Amendment. However, the Commissioner is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 13-2855, under Order No. 28385/35415.

Respectfully submitted,

MARSHALL, GERSTEIN & BORUN LLP

August 22, 2005

Michael F. Borun, Reg. No. 25,447
Attorney for Applicant
6300 Sears Tower
233 S. Wacker Drive
Chicago, Illinois 60606-6357
(312) 474-6300